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EXAMINER	
BALLARD, KIMBERLY	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,905	KORTH ET AL.	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *22,24-27 and 31-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,23 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/04/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claim 23 and each of claims 1-21 in part, drawn to an antibody termed 9C9 that can be produced by hybridoma cells deposited as DSM ACC2714, in the reply filed on February 19, 2010 is acknowledged. The traversal is on the ground(s) that contrary to the prior art teachings of Roulea et al. (WO 00/26675), experiments conducted by Applicant have indicated that the polyglutamine-containing proteins taught by Roulea et al. do not occur at elevated concentrations in schizophrenia patients and thus cannot be used as diagnostic markers for schizophrenia. Applicant asserts that they are the first to determine that the presence of misfolded proteins can serve as a diagnostic marker of schizophrenia or other neuropsychiatric diseases, such as depression or bipolar affective disorders. This is not found persuasive because the first recited technical feature of the present claims is that of an antibody that recognizes misfolded proteins, which is taught by the prior art reference of Roulea et al. The recited limitations of "for the diagnosis or treatment of neuropsychiatric diseases" is not given patentable weight because these are considered intended uses of the claimed antibody and do not structurally limit the claimed antibody molecule. Therefore, whether or not Applicant have been able to replicate the findings of Roulea et al. is irrelevant to the instant situation, because Roulea clearly discloses an antibody that recognizes misfolded and aggregated proteins. Accordingly, as discussed previously, the technical feature linking the inventions of Groups I-VI does not constitute

a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

However, the examiner notes that amended claims 28-30 read upon the elected invention. Therefore, the restriction requirement between groups II and IV only is hereby vacated.

The requirement is still deemed proper and is therefore made FINAL.

2. Accordingly, claims **1-21, 23** and **28-30**, to the extent they are drawn to the antibody termed 9C9, are under examination in the present office action.

Information Disclosure Statement

3. The information disclosure statement (IDS) filed October 4, 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the IDS is completely blank, i.e., there are no citations listed and it is neither signed nor dated. It has been placed in the application file, but because there is no information referred to therein, there is nothing for the examiner to consider. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

4. Claims 1-21 and 23 are objected to because of the following informalities: products such as antibodies are conventionally recited as “An antibody” in independent claims (such as in claims 1 and 23) and “The antibody” in dependent claims (such as in claims 2-21). Appropriate correction is respectfully suggested.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-13, 17 and 19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Specifically, the claims are directed to an antibody that recognizes misfolded proteins. It is noted that the limitations reciting that the antibody is for the diagnosis or treatment of neuropsychiatric diseases, do not serve to distinguish the claimed antibody from those which occur in nature, such as those antibodies that are still in a living being. For example, the presence of autoantibodies directed against a misfolded protein in patient having a neuropsychiatric disease could be used to diagnosis the patient. Additionally, all of the limitations recited in claims 6-13 are with respect to purification of the protein used to immunize an animal for production of the claimed antibody, wherein the antibody itself would still be in its natural state in the immunized animal. It is also noted that inclusion of the phrase "isolated" or “purified” would overcome this rejection.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 23, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-21 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to an antibody that recognizes misfolded proteins that can be assigned specifically to a neuropsychiatric disease, wherein the disease may be

schizophrenia (claim 2), depression (claim 3), or bipolar affective disorder (claim 3), or wherein the antibody recognizes misfolded proteins that are specific for multiple diseases, whereby the assignment to a disease can be made by means of further properties of the protein and/or by means of its origin (claim 5). The claims are thus directed to a genus of antibodies that recognize a genus of undefined proteins associated with a genus of diseases, and are therefore considered genus claims. The specification hypothesizes the misfolded protein(s)' existence and posits a screening assay which could be performed to identify antibodies or antibody fragments that recognize the misfolded proteins (such as at page 6 of the specification). Here, applicant has not described the structures of a reasonable number of members of the genus now claimed, but rather has presented the public with an idea of how to perform an assay that might identify some agents that fall within the scope of the claim. Of course, depending on which antibodies are tested in the screening assay, there may in fact be no antibodies actually identified for diagnostic or therapeutic use.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Applicants are directed to the recently-published guidelines on interpretation of the written description requirement, available on the internet at: http://www.uspto.gov/web/menu/written.pdf . See in particular Example 14, regarding antibodies directed to a genus of proteins.

The specification describes the production of three monoclonal antibodies, 7B2, 9C9 and RC1, that were obtained by the immunization of animals with protein isolated from brain homogenates from patients having schizophrenia and/or were identified as recognizing pelleted protein homogenates from schizophrenia brain samples. Antibodies 7B2 and 9C9 are noted to have deposit accession numbers (see page 26), whereas no such information is provided for the antibody RC1. However, these limited examples of antibodies directed to misfolded proteins from one neuropsychiatric disorder (schizophrenia) do not provide adequate description for the genus of antibodies capable of recognizing numerous disease-associated proteins, wherein no detailed structural information is provided for such proteins and wherein the misfolded proteins may be associated with *any* disease. The specification does not describe a complete or partial structure of an antibody capable of recognizing a misfolded disease-associated protein in detailed drawings or through a structural chemical formula. Further the spec does not disclose a correlation between such misfolded proteins and the structure of the claimed antibody.

Other than the 7B2, 9C9 and RC1 antibodies that recognize pelleted proteins obtained from brain homogenates of schizophrenic patients, the specification does not provide sufficient guidance as to the structural characteristics of agents capable of recognizing the diverse and ill-defined genus of misfolded disease-associated proteins encompassed by the claimed invention. Given the well known high level of polymorphism of immunoglobulins / antibodies, the skilled artisan would not have recognized that Applicant was in possession of the vast repertoire of antibodies and

antibody fragments encompassed by the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus nor guidance as to which of myriad of antibodies that are encompassed by the claimed binding agents would be effective in the diagnosis or treatment of neuropsychiatric diseases.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed antibodies, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identification and isolation of such antibodies. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 (BPAI 1993). In *Fiddes*, claims directed to mammalian FGF's

were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the 9C9, 7B2 or RC1 monoclonal antibodies, but not the full breadth of the claims, meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

11. Claim 1-21, 23, and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Regarding claim 23, the claim is drawn to an antibody termed 9C9 that can be produced by hybridoma cells that are deposited under the number DSM ACC2714, for

diagnosis or treatment of diseases, in particular of neuropsychiatric diseases, such as schizophrenia or depression or bipolar disorder.

The process of producing monoclonal antibodies is unpredictable; even when a small antigen is used multiple different monoclonal antibodies can be produced. See for example Kuby (1997. Immunology, Third Edition, pp. 131 - 134), which teaches the process by which monoclonals are produced. See also Alberts et al. (2002. Molecular Biology of the Cell, 3rd Edition, pp. 1216 - 1220). Alberts teaches the three-dimensional structure of antibodies is complex. Note particularly the large models on pp. 1219 - 1220 which indicate that the antibody molecules are comprised of hundreds of amino acids. The structure of a large protein such as an antibody is dependent not just on the antigen-binding region, but on the totality of the interactions of the hundreds of amino acid residues.

The specification fails to disclose the complete sequence and structure of monoclonal antibody 9C9, which is specifically recited by claim 23. The art recognizes that making monoclonals is an unpredictable process. Monoclonal antibodies are so unique that a skilled artisan cannot simply construct one, the actual hybridoma which secretes the antibody must be present in order to make it. Thus deposit of said hybridoma is required for compliance with § 112, first paragraph. MPEP § 2404.02 recognizes that when undue experimentation would be required for an artisan to make a biological product, deposit can be required. The examiner has concluded that in order to make the actual antibody 9C9, the hybridoma is required.

Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification lacks sufficient deposit information for the monoclonal antibody 9C9. Because this monoclonal antibody is unknown, and therefore, publicly not available and cannot be reproducibly isolated from nature without undue experimentation, a suitable deposit for patent purposes is required. The 9C9 mAb would not be expected to be reliably reproduced from any and all immunizations with insoluble protein pellets obtained from brain homogenates from schizophrenia patients.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or

her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be **irrevocably removed** upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements. For the reasons above, it would not be possible for the skilled artisan to make and use the antibody recited in claim 23.

Regarding claims 1-21 and 28-30, antibodies other than 9C9 and the antibodies of prior art Rouleau et al. and Cashman et al. (see below) are also not enabled for the following reasons.

In the instant case, the nature of the invention is complex. In general, the claims are drawn to an antibody that recognizes an extremely broad genus of disease-

associated proteins and, as stated above, Applicants have not described all of the common features of the genus of antibodies or the proteins to which they bind such that the skilled artisan could identify individual members. Applicants have not provided sufficient guidance, for example by showing a correlation between structural characteristics and the desired functional effect, to allow one of skill in the art to use the claimed invention with any antibody which meets the limitations of the claims. The claims also recite the use of the antibodies for diagnostic or therapeutic purposes, such as in pharmaceutical preparations. The sole examples are directed to specific monoclonal antibodies 7B2, 9C9 and RC1, which demonstrate their use in *in vitro* diagnostic assays. In particular, the antibodies were demonstrated to recognize protein bands in brain homogenates from patients having schizophrenia, but not from normal control subjects. At best, therefore, these specific antibodies could potentially be used in conjunction with clinical assessment to confirm a diagnosis of schizophrenia. There is no evidence, however, that any of the antibodies would useful for the detection/diagnosis of other mental disorders, such as depression or bipolar affective disorder, nor for the treatment of these diseases. Also, in the absence of a deposit, the specification fails to teach how to make these specific antibodies. See discussion above regarding biological deposits.

While the skill level in the art is high, the level of predictability is low. Applicant's invention is predicated on the finding that non-soluble fractions of brain homogenates (comprising misfolded proteins) can be detected in brain samples from patients having schizophrenia and therefore can be used as an indicator of the disease. Applicant

extrapolates this result into an antibody for use in the treatment of neuropsychiatric diseases and/of for the diagnosis of any neuropsychiatric disease. Thus it would appear that Applicant provides a single finding and then presents an invitation to experiment to determine how to use the antibodies therapeutically. The instant specification provides no working examples pertaining to the use of any such antibody for therapeutic use. In general, the art is silent with respect to the involvement of misfolded proteins in the pathology of neuropsychiatric diseases. And even if such proteins were associated with the psychiatric disorders of schizophrenia, depression, and bipolar affective disorder, there is no evidence of record to indicate that these proteins are causative factors in the initiation or propagation of the disorder. In other words, the finding that aggregated proteins exist in the brains of schizophrenic patients does not necessarily mean that removal or inhibition of these proteins (such as with the antibodies) will have any therapeutic effect whatsoever on the patient. The production of these proteins could, for example, be a compensatory mechanism by which the brains of patients having schizophrenia attempt to counterbalance or correct for other neurochemical deficiencies and/or abnormalities. Therefore, it is possible that inhibition and/or clearance of these proteins could in fact exacerbate the neuropsychiatric disease. In the absence of a clear nexus between the role of one or more of the misfolded brain proteins and the pathogenesis of a specific neuropsychiatric disease, undue experimentation would be required of the skilled artisan to use the claimed antibodies in therapeutically.

In order to practice the full scope of the claimed invention, the skilled artisan would have to discover, on his or her own, the antibodies which are capable of reliably diagnosing various neuropsychiatric diseases as well as determining whether such antibodies could be used for the treatment of such diseases. These are required starting materials for the claimed methods, but the specification does not teach the artisan how to use the full scope of these materials. While it is possible that the artisan could perform a screening assay to identify such antibodies, this is not sufficient to indicate how to actually use the claimed antibodies in the full scope of their diagnostic or therapeutic potential. Thus the artisan would have to resort to undue experimentation to determine how to use the claimed antibodies, as the artisan would have to invent or discover the antibodies on his or her own.

The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary to determine how to use the claimed antibodies for the diagnosis of diseases other than schizophrenia or for the treatment of any neuropsychiatric disease, the lack working examples directed to same, and the paucity

of guidance commensurate in scope with the large breadth of the claims, undue experimentation would be required of the skilled artisan to use the invention commensurate in scope with the claimed product.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1-14, 16-18 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/26675 by Rouleau et al. (published 11 May 2000; cited previously).

The claims recite an antibody for the diagnosis or treatment of neuropsychiatric diseases, wherein the antibody recognizes misfolded proteins that can be assigned specifically to one of the diseases. However, the recitation of "for the diagnosis or treatment of neuropsychiatric diseases" does not confer any patentable weight because it appears solely in the preamble. A preamble is generally not accorded patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for

completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See also MPEP § 2111.02, section II. Accordingly, the broadest reasonable interpretation of the claims is that of an antibody that recognizes a disease-associated misfolded protein(s).

Rouleau et al. disclose aggregated polyglutamine-containing proteins that are markers of neuropsychiatric disorders, such as schizophrenia and major depression, and in particular antibodies that specifically recognize these proteins (see p. 3, lines 5-9 and paragraph spanning pp. 3-4), thus addressing recited limitations of present claims 1-3 and 5. Regarding claim 4, Rouleau defines "neuropsychiatric disorders" as inclusive of manic depression illness, which is synonymous with bipolar affective disorder.

Regarding claims 6-13, it is noted that all of the recited limitations are drawn to the enrichment of the protein used to immunize animals with to obtain the claimed antibody. All of these limitations are considered product-by-process limitations, where by the process by which the antibody is obtained does not in fact change the claimed product, which is an antibody that recognizes a misfolded disease-associated protein. See MPEP § 2113, which states that:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

With respect to claims 14, 16 and 18, Rouleau teaches monoclonal, humanized and chimeric antibodies at p. 18 (lines 3-13), and the specific monoclonal antibody 1C2 at p. 3 for example. Humanized and chimeric antibodies are species of recombinant antibodies, and would therefore anticipate claim 16 which recites that the antibody is a recombinant antibody.

And finally regarding claims 17 and 28, Rouleau discloses pharmaceutically acceptable preparations comprising the antibodies of the invention in an amount effective to achieve the desired therapeutic effect (see paragraph spanning pp. 18-19). Because Rouleau's disclosure relates to the treatment of neuropsychiatric disease, including schizophrenia, and because neuropsychiatric disease involves the brain, in order to achieve therapeutic efficacy the administered agent would necessarily have to cross the blood brain barrier. Therefore, the therapeutic agents disclosed by Rouleau, which include antibodies, would be expected to inherently be in a blood-brain-barrier crossing form.

14. Claims 1, 5-16 and 18-21 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 2005/019828 A1 by Cashman et al. (filed 20 August 2004, priority to 20 August 2003) as evidenced by Wall et al. (*J Neuropsychiatry Clin Neurosci*. 2005; 17(4):489-95).

As noted above, the present claims are directed to an antibody that recognizes misfolded proteins that can be assigned specifically to a neuropsychiatric disease. The present specification at pages 3-4, paragraph [0011], defines "neuropsychiatric disease"

as covering “in particular psychoses, including organic psychoses, i.e., diseases comprising classical features of psychosis as symptoms (delusion, hallucination, impairment of thought, mood changes or other affective symptoms and cognitive disorders).”

Cashman et al. disclose antibodies that are capable of recognizing conformational epitopes on disease-associated polypeptides. Cashman teaches that protein misfolding can cause protein aggregation which can further give rise to discrete extracellular or intracellular deposits, wherein diseases such as Alzheimer's disease, Parkinson’s disease, Huntington's disease, amyotrophic lateral sclerosis and prion diseases are characterized by neural deposits of such misfolded aggregated protein (see p. 1). In particular, Cashman provides for methods of detecting prion diseases, comprising the use of an antibody specific for a target epitope on the prion protein (see p. 10), such as for detecting the non-wild type conformation (i.e., disease associated) conformation of the prion protein, PrP^{Sc} (see p. 20). Cashman teaches, for example, that the “non-wildtype conformation” refers to a conformation of polypeptide that differs from the conformation of the wild type polypeptide and can include a conformation of a polypeptide in a disease or disorder, wherein the difference in conformation may be a result of differential folding, polypeptide aggregation or differential post-translational modification compared to the wild type polypeptide (see p. 27). Thus, antibodies that recognize the non-wild type conformation of the disease-associated polypeptide would be conformation-specific antibodies.

Wall et al. evidence that symptoms of Creutzfeldt-Jakob disease (CJD), which is a human prion disease, include psychiatric manifestations, including psychotic symptoms (disorganized thought processes, delusions and paranoia), depression, behavioral dyscontrol/agitation, sleep disturbances and anxiety (see, for example, Table 3 on p. 491), wherein over 90% of patients manifest at least one psychiatric symptom during the course of the illness (see p. 492, 1st column). Wall also notes that a large percentage of patients having Alzheimer's disease (AD) or Lewy body dementia (LBD) also report psychotic manifestations such as hallucinations and delusions (see p. 493, 1st column). Therefore, as evidenced by Wall et al., prion diseases such as CJD and dementing illnesses such as AD and LBD, as disclosed by Cashman would meet the limitation of a "neuropsychiatric disease" as defined by the present specification and recited in claim 1.

Regarding claim 5, it is noted that certain misfolded proteins, such as alpha-synuclein, are present in numerous diseases such as Parkinson's disease, LBD and AD (see p. 5). Therefore, the antibodies directed to such proteins would recognize "misfolded proteins that are specific for multiple diseases", as recited in the claim 5, especially in view of the fact that there is nothing recited in the claim to limit the "multiple diseases" to neuropsychiatric diseases.

Regarding claims 6-13, it is noted that all of the recited limitations are drawn to the enrichment of the misfolded protein used to immunize animals with to obtain the claimed antibody. All of these limitations are considered product-by-process limitations, where by the process by which the antibody is obtained does not in fact change the

claimed product, which is an antibody that recognizes a misfolded disease-associated protein. See MPEP § 2113, which states that:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

With respect to claims 14-16, 18 and 19, Cashman teaches monoclonal and chimeric antibodies as well as antibody fragments at p. 40. Examples of monoclonal antibodies specific for particular conformational epitopes of disease-associated misfolded proteins are given at p. 39. Chimeric antibodies are a species of recombinant antibodies, and would therefore anticipate claim 16 which recites that the antibody is a recombinant antibody.

And regarding claims 20 and 21, Cashman discloses that antibodies may be labeled with a detectable substance, including radioisotopes (see p. 42).

Conclusion

15. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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